IN THE NEWS

DNA goes private

Worried you might not be the biological father of your child? Or are you an unscrupulous journalist chasing a scoop on an unfaithful celebrity? Today, nothing prevents you from collecting DNA from, say, a coffee mug, and analysing it. "The possibility that people may obtain samples without consent lies behind one of [the] main recommendations of the Human Genetics Commission [HGC]" (*The Guardian*), a UK government advisory body that published a major report on the use and storage of genetic data in May. If the HGC has its way, it will be illegal to "deceitfully obtain and analyse another person's genetic information for non-medical purposes" (*BBC News*), helping to curb genetic discrimination at work, for example. An "exception would apply to the police, who could legally obtain, analyse and store DNA samples without consent" (*New Scientist*).

David King, of the pressure group Human Genetics Alert, accused the commission of "pulling its punches." It "failed to back a legislative ban on discrimination, merely calling for the Government to consider such a ban", he said (*The Times*). "I am reminded of Sherlock Holmes' case of the watchdog that did not bark" (*The Guardian*).

Independent bodies would "oversee DNA databases used by the police and by medical researchers to prevent Britain becoming a "Big Brother" state" (*The Guardian*). This has implications for projects such as Biobank UK, a database that will eventually contain DNA samples from 500,000 volunteers. Outlawing "covert testing would put the UK ahead of other countries", said one commissioner. "While it may not stop covert tests it may force people to think twice before doing it" (*BBC News*).

Tanita Casci

SEX DETERMINATION

Sexing medaka

Compared with other fish, sex determination in medaka has been closely scrutinized. Homologous targets of *Sry* — the mammalian gene that directs male development — are known in medaka, but it is only now that a non-mammalian candidate counterpart of *Sry* that is required for male development has been found.

Matsuda and colleagues positionally cloned the sex-determining region by constructing a Y-congenic strain to differentiate between the similar medaka sex chromosomes. The strain carries a sex-linked pigment gene that makes XX females white and XY males orange-red. The sex-determining region was then mapped by recombination between it and the pigment loci, and was narrowed down thanks to an XY orange-red female that lacked 250 kb on the Y. Only one ORF in this interval, *DMY*, was specifically expressed in male embryos, in the somatic gonad.

***DMY* contains the highly conserved DM domain, which is found in many developmentally important genes, including sex-determining genes. Two naturally occurring sex-reversal mutants, in which *DMY* is either truncated or expressed at reduced levels,**

X INACTIVATION

Finding the X factor(s)

The life of an embryonic cell is full of choices — become this or that, stay put or migrate. In female mammals, a fundamental choice is which X chromosome to inactivate during early development. Traditionally, the X-inactivation centre (*Xic*), a region on the X chromosome, was believed to control this decision, but now Ivona Percec and colleagues provide the first genetic evidence that autosomal loci also influence this choice.

In mice, the *Xic* consists of three main elements: *Xist*, an untranslated RNA transcribed from the inactive X (X_i) that initiates and propagates silencing *in cis*; *Tsix*, the antisense transcript of the *Xist* locus that is transcribed from the active X (X_a) and represses *Xist in cis* before the initiation of X inactivation; and the X controlling element (*Xce*). *Xce*, along with other regions in the *Xic*, determines which of the two X chromosomes to inactivate. However, it has long been suspected that not all of the factors involved in this elusive step are on the X chromosome.

To find these factors, Percec *et al.* did a mouse phenotypic screen in which they exploited the effects of different *Xce* alleles on X-inactivation patterns. They used a 'strong' *Xce* (Xce^c) allele, which is more likely to be on the X_a (from the *Mus musculus castaneous* strain), and 'weak' *Xce* (Xce^a and Xce^b) alleles, which are more likely to be on the X_i (from *M. m. musculus*). In $Xce^{a/c}$ and $Xce^{b/c}$ heterozygous females, 25–30% of cells keep active the X chromosome that carries the strong Xce^c allele. In the screen, heterozygous $Xce^{a/c}$ and $Xce^{b/c}$ females were identified in the progeny of ENU-mutagenized *M. m. musculus* males and screened for changes in their expected X-inactivation patterns, as were their female progeny.

From this screen, two females (1.19 and 24.21) with this phenotype were identified. In both pedigrees, carrier females inactivated the Xce^c-bearing chromosome in more cells than expected. This altered pattern was dominantly and stably inherited. It also occurred independently of genetic background and early in development, indicating that the mutations have a primary effect on X inactivation. Importantly, the altered X-inactivation patterns did not segregate with the mutagenized X chromosome, indicating their autosomal inheritance.

Next, the authors did a genome scan in pedigree 24.21 by tracing the inheritance of the mutagenized founder male's alleles. All of these markers segregated independently of the mutant phenotype, except for those on the proximal half of chromosome 15, a region not known to